

This listing of claims will replace all prior versions and listing of claims in the application.

Claims 1-22 (canceled)

23. (Previously amended) The compound of Claim 41 wherein R¹ is hydrogen, C₁₋₄alkyl, C₁₋₄alkoxy, halogen or CF₃.

24. (Previously amended) The compound of Claim 41 wherein R² is hydrogen, C₁₋₄alkyl, C₁₋₄alkoxy, halogen or CF₃.

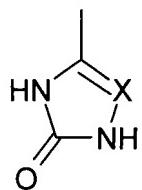
25. (Previously amended) The compound of Claim 41 wherein R³ is hydrogen, fluorine, chlorine or CF₃.

26. (Previously amended) The compound of Claim 41 wherein R⁴ is hydrogen or fluorine.

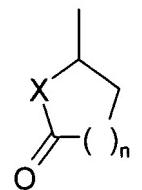
27. (Previously amended) The compound of Claim 41 wherein R⁵ is hydrogen, fluorine, chlorine or CF₃.

28. (Previously amended) The compound of Claim 41 wherein R⁶ is C₁₋₄alkyl optionally substituted by hydroxy.

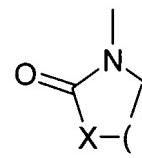
29. (Previously amended) The compound of Claim 41 wherein R⁷ is a cyclic group selected from the group consisting of:



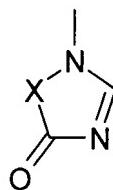
X is N, CH or CH₂



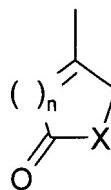
X is O or CH₂
n is 1 or 2



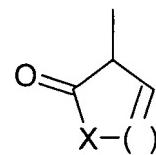
X is O, NH, CH₂ or NR¹³
n is 1 or 2



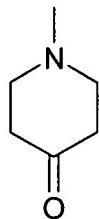
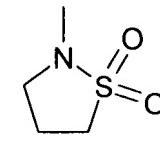
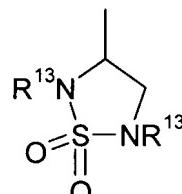
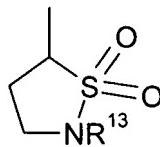
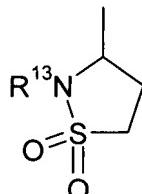
X is NH or CH₂



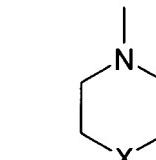
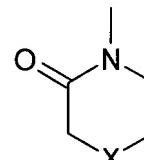
X is O, NH, CH₂ or NR¹³
n is 1 or 2



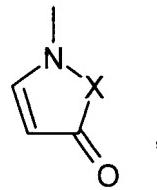
X is O, NH, CH₂ or NR¹³
n is 1 or 2



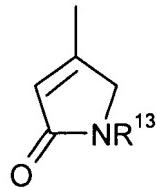
X is NR¹³ or CH₂



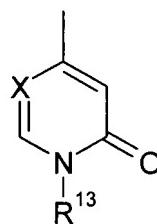
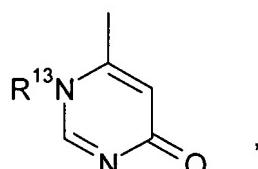
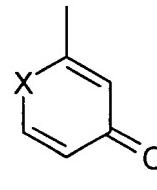
X is NR¹³ or CH₂



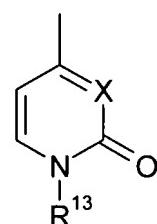
X is NR¹³ or CH₂



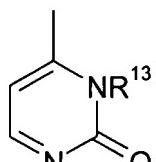
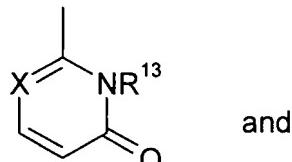
X is NR¹³, O or SO₂



X is N or CH



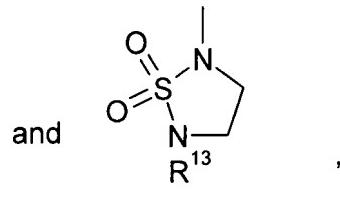
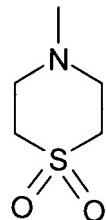
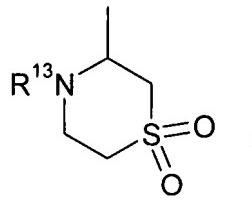
X is N or CH



X is N or CH

wherein any of said cyclic groups is unsubstituted or substituted by one or more groups as defined in Claim 22 Claim 41.

30. (Currently amended) The compound of Claim 22 Claim 41 wherein R⁷ is a cyclic group selected from the group consisting of:



Wherein any of said cyclic groups is unsubstituted or substituted by one or more groups as defined in Claim 4 Claim 41.

31. (Previously amended) The compound of Claim 41 wherein R⁸ is hydrogen or methyl.

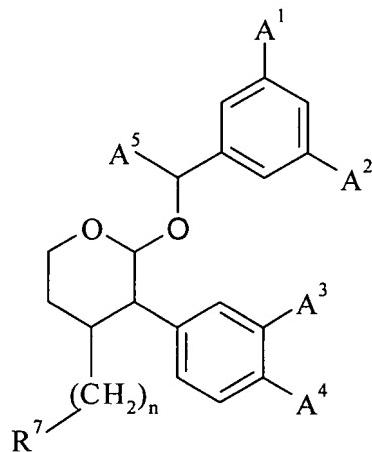
32. (Previously amended) The compound of Claim 41 wherein R¹² is hydrogen, hydroxy, C₁₋₂alkyl substituted by hydroxy, C₁₋₄alkoxy or CO₂R^e, where R^e is hydrogen, methyl ethyl or benzyl.

33. (Previously amended) The compound of Claim 41 wherein R¹³ represents hydrogen, methyl or ethyl.

34. (Previously amended) The compound of Claim 41 wherein R¹⁵ is hydrogen and R¹⁶ is hydrogen.

35. (Previously amended) The compound of Claim 41 wherein n is zero or 1.

36. (Previously amended) The compound of Claim 41 of the formula (Ia):



(Ia)

wherein:

A¹ is fluorine or CF₃;

A² is fluorine or CF₃;

A³ is fluorine or hydrogen;

A⁴ is fluorine or hydrogen;

A⁵ is methyl;

or a pharmaceutically acceptable salt thereof.

37. (Previously added) A compound which is selected from the group consisting of:
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]piperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-methylpiperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-ethylpiperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-(1-methylethyl)piperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-cyclohexylpiperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-(tetrahydropyran-4-yl)piperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-(1-methylpiperidin-4-yl)piperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-phenylpiperazinone;
- 1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-4-(pyrid-3-yl)piperazinone;
- 4-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]piperazinone;
- 4-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-1-methylpiperazinone;
- 4-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-1-ethylpiperazinone;
- 4-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-1-phenylpiperazinone;
- 4-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-1-(pyrid-3-yl)piperazinone;

Serial No.: 10/521,338

Case No.: T1587P

Page 7

4-[((2*R*,3*S*,4*S*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]piperazinone;

4-[((2*R*,3*S*,4*S*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-1-methylpiperazinone;

4-[((2*R*,3*S*,4*S*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2*H*-pyran-4-yl)methyl]-1-ethylpiperazinone;

4-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(3,4-difluorophenyl)-2*H*-pyran-4-yl)methyl]thiomorpholine 1,1-dioxide;

4-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]thiomorpholine 1,1-dioxide;

1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]-2-pyrrolidinone;

1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]-2,5-pyrrolidinedione;

1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]-2-imidazolidinone;

1-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]-3-methyl-2-imidazolidinone;

3-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]-1-methyl-2,4-imidazolidinedione;

2-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]-5-ethyl-1,2,5-thiadiazolidine 1,1-dioxide;

(*5R* or *S*)-5-((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)-2,4-imidazolidinedione;

(*3R* or *S*)-3-((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)-4-methylthiomorpholine 1,1-dioxide;

2-[((2*R*,3*R*,4*R*)-2-{(1*R*)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-phenyl-2*H*-pyran-4-yl)methyl]isothiazolidine 1,1-dioxide;

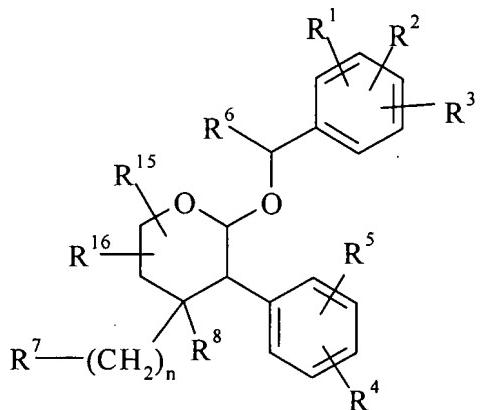
or a pharmaceutically acceptable salt thereof.

38. (Previously amended) A pharmaceutical composition comprising the compound of Claim 41 and at least one pharmaceutically acceptable carrier or excipient.

39. (Previously amended) A method for the treatment of pain or inflammation, migraine, emesis, postherpetic neuralgia, depression or anxiety, which method comprises administration to a patient in need thereof of a therapeutically effective amount of the compound of Claim 41.

40. (Previously amended) A method for the prevention of pain or inflammation, migraine, emesis, postherpetic neuralgia, depression or anxiety, which method comprises administration to a patient in need thereof of a therapeutically effective amount of the compound of Claim 41.

41. (Previously added) A compound of the formula (I):



(I)

wherein:

R^1 is hydrogen, halogen, C₁₋₆alkyl, C₁₋₆alkoxy, fluoroC₁₋₆alkyl, fluoroC₁₋₆alkoxy, C₃₋₇cycloalkyl, C₃₋₇cycloalkylC₁₋₄alkyl, NO₂, CN, SR^a, SOR^a, SO₂R^a, CO₂R^a, CONR^aR^b, C₂₋₆alkenyl, C₂₋₆alkynyl or C₁₋₄alkyl substituted by C₁₋₄alkoxy, wherein R^a and R^b each independently represent hydrogen or C₁₋₄alkyl;

R^2 is hydrogen, halogen, C_{1-6} alkyl, fluoro C_{1-6} alkyl or C_{1-6} alkoxy substituted by C_{1-4} alkoxy;

R^3 is hydrogen, halogen or fluoroC₁₋₆alkyl;

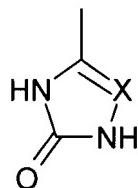
R^4 is hydrogen, halogen, C₁₋₆alkyl, C₁₋₆alkoxy, fluoroC₁₋₆alkyl, fluoroC₁₋₆alkoxy, hydroxy, NO₂, CN, SR^a, SOR^a, SO₂R^a, CO₂R^a, CONR^aR^b, C₂₋₆alkenyl, C₂₋₆alkynyl or C₁₋₄alkyl substituted by C₁₋₄alkoxy;

R^5 is hydrogen, halogen, C₁₋₆alkyl, fluoroC₁₋₆alkyl or C₁₋₆alkoxy substituted by C₁₋₄alkoxy;

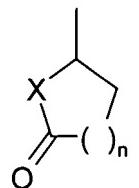
R^6 represents hydrogen or a C₁₋₄alkyl group which is unsubstituted or substituted by a hydroxy group;

R^7

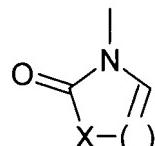
is a cyclic group selected from the group consisting of:



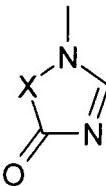
X is N, CH or CH₂



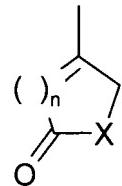
X is O or CH₂
n is 1 or 2



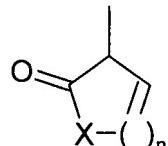
X is O, NH, CH₂ or NR¹³
n is 1 or 2



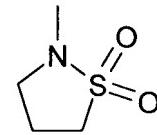
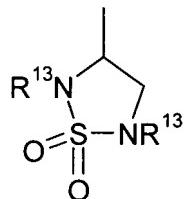
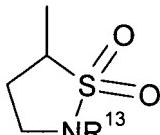
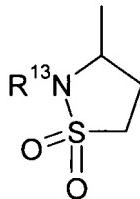
X is NH or CH₂

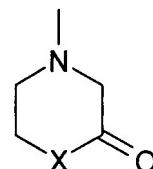
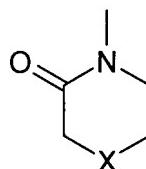
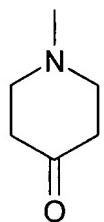
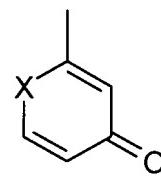
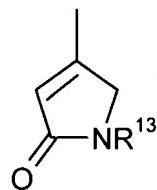
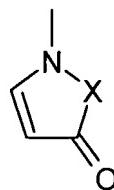
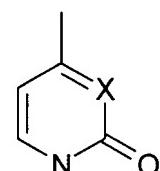
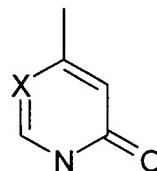
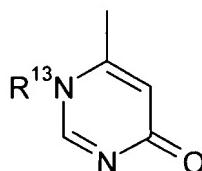


X is O, NH, CH₂ or NR¹³
n is 1 or 2



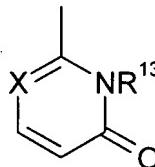
X is O, NH, CH₂ or NR¹³
n is 1 or 2



X is NR¹³ or CH₂X is NR¹³ or CH₂X is NR¹³ or CH₂X is NR¹³, O or SO₂

X is N or CH

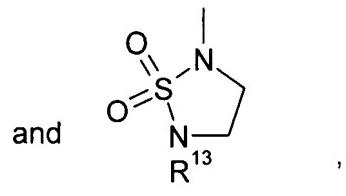
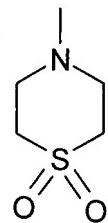
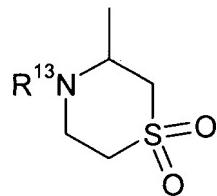
X is N or CH



and



X is N or CH



and

wherein cyclic group is unsubstituted or substituted at any substitutable position by one or more substituents selected from =O, halogen, hydroxy, R¹¹, R¹², SR^f, SO₂R^g, COR^a, CO₂R^a, CONR⁹R¹⁰,

-ZNR⁹R¹⁰, benzyl, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, fluoroC₁₋₄alkyl, chloroC₁₋₄alkyl, C₁₋₄alkoxyC₁₋₄alkyl, C₃₋₇cycloalkyl, C₃₋₇cycloalkylC₁₋₄alkyl, C₃₋₇cycloalkoxy, C₃₋₇cycloalkoxyC₁₋₄alkyl, C₁₋₄alkoxy, fluoroC₁₋₄alkoxy, hydroxyC₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkoxy, aryl, arylC₁₋₄alkyl, heteroaryl, heteroarylC₁₋₄alkyl or a 5- or 6-membered ring containing in the ring one oxygen atom or N(C₁₋₆alkyl), wherein R^f is C₁₋₄alkyl or aralkyl or aryl and R^g is C₁₋₄alkyl, aryl, arylC₁₋₄alkyl or NR⁹R¹⁰;

R⁸ represents hydrogen, C₁₋₆alkyl, fluoroC₁₋₆alkyl, hydroxy, C₁₋₆alkoxy, hydroxyC₁₋₆alkyl NR⁹R¹⁰, CONR⁹R¹⁰ or SO₂R^g;

R⁹ is hydrogen, C₁₋₄alkyl, C₃₋₇cycloalkyl, C₃₋₇cycloalkylC₁₋₄alkyl, fluoroC₁₋₄alkyl, C₂₋₄alkyl substituted by a C₁₋₄alkoxy or hydroxyl group, or R⁹ is a five membered or six membered nitrogen-containing heteroaromatic ring as previously defined;

R¹⁰ is hydrogen or C₁₋₄alkyl, C₃₋₇cycloalkyl, C₃₋₇cycloalkylC₁₋₄alkyl, fluoroC₁₋₄alkyl or C₂₋₄alkyl substituted by a C₁₋₄alkoxy or hydroxyl group;

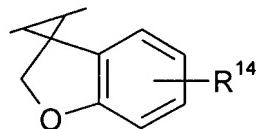
or R⁹, R¹⁰ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms, unsubstituted or substituted by one or two groups selected from hydroxy, COR^e, CO₂R^e, C₁₋₄alkyl unsubstituted or substituted by a C₁₋₄alkoxy or hydroxyl group, or C₁₋₄alkoxy unsubstituted or substituted by a C₁₋₄alkoxy or hydroxyl group, or a five membered or six membered nitrogen-containing heteroaromatic ring as previously defined, or said heteroaliphatic ring is substituted by a spiro-fused lactone ring, and said heteroaliphatic ring optionally containing a double bond, which heteroaliphatic ring may contain an oxygen or sulphur ring atom, a group S(O) or S(O)₂ or a second nitrogen atom which will be part of a NH or NR^d moiety, where R^d is C₁₋₄alkyl unsubstituted or substituted by hydroxy or C₁₋₄alkoxy;

or R⁹, R¹⁰ and the nitrogen atom to which they are attached form a non-aromatic azabicyclic ring system of 6 to 12 ring atoms;

or R⁹, R¹⁰ and the nitrogen atom to which they are attached form a heteroaliphatic ring of 4 to 7 ring atoms to which is fused a benzene ring or a five membered or six membered nitrogen-containing heteroaromatic ring optionally containing 1, 2 or 3 additional heteroatoms selected from N, O and S;

R¹¹ and R¹² each independently represent hydrogen, hydroxy, COR^e, CO₂R^e, C₁₋₄alkyl unsubstituted or substituted by a C₁₋₄alkoxy or hydroxyl group, or C₁₋₄alkoxy unsubstituted or substituted by a C₁₋₄alkoxy or hydroxyl group;

or, when they are attached to the same carbon atom, R¹¹ and R¹² may together represent =O, =CHCO₂R^a, -O(CH₂)_mO-, -CH₂O(CH₂)_k-, -CH₂OCH₂C(O)-, -CH₂OCH₂CH(OH)-, -CH₂OCH₂C(CH₃)₂-, -CH₂OC(CH₃)₂CH₂-, -C(CH₃)₂OCH₂CH₂-, -CH₂C(O)OCH₂-, -OC(O)CH₂CH₂-, -C(O)OCH₂CH₂-, -C(O)OC(CH₃)₂CH₂-, -C(O)OCH₂C(CH₃)₂-, -OCH₂(CH₂)_k-, -OC(CH₃)₂CH₂CH₂-, -OCH₂C(CH₃)₂CH₂-, -OCH₂CH₂C(CH₃)₂-, -OCH₂CH=CHCH₂-, -OCH₂CH(OH)CH₂CH₂-, -OCH₂CH₂CH(OH)CH₂-, -OCH₂C(O)CH₂CH₂-, -OCH₂CH₂C(O)CH₂-, or a group of the formula:



or, where they are attached to adjacent carbon atoms, R¹¹ and R¹² may together represent -OCH₂CH₂- or -OCH₂CH(OH)-, or R¹¹ and R¹² may together form a fused benzene ring;

or, R¹¹ and R¹² together form a C₁₋₂alkylene bridge across the pyrrolidine, piperidine, morpholine or piperazine ring to which they are attached;

R¹³ represents hydrogen, phenyl, benzyl, pyridyl, tetrahydropyranyl, piperidinyl, N-substituted piperidinyl (where the N-substituent is C₁₋₆alkyl), C₁₋₄alkyl, C₃₋₇cycloalkyl, C₃₋₇cycloalkylC₁₋₄alkyl, -SO₂C₁₋₄alkyl or C₂₋₄alkyl substituted by a C₁₋₄alkoxy or hydroxyl group;

R¹⁴ represents hydrogen, halogen, hydroxy, C₁₋₄alkyl, hydroxyC₁₋₄alkyl or fluoroC₁₋₄alkyl;

R¹⁵ and R¹⁶ each independently represent hydrogen, halogen, C₁₋₆alkyl, CH₂OR^c, oxo, CO₂R^a or CONR^aR^b where R^a and R^b are as previously defined and R^c represents hydrogen, C₁₋₆alkyl or phenyl;

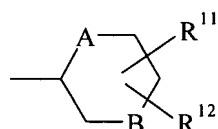
Z represents a bond, C₁₋₆alkylene or C₃₋₆cycloalkylene;

k is 1, 2 or 3;

m is 1 or 2; and

n is zero, 1 or 2;

with the proviso that when n is zero and R⁸ is hydrogen, R⁷ does not represent a C-linked nitrogen-containing ring of the formula:



wherein:

Serial No.: 10/521,338

Case No.: T1587P

Page 13

A represents NR¹³, and B represents a bond, CH₂, NR¹³ or O, wherein one or both hydrogen atoms in said CH₂ moiety may be replaced with one or both of R¹¹ and R¹², or alternatively, one of the hydrogen atoms in said CH₂ moiety together with a hydrogen atom from an adjacent carbon are replaced by a double bond; or A is O, and B is NR¹³; and R¹¹ and R¹² together represent =O; and pharmaceutically acceptable salts thereof.

42. (New) A compound of claim 41 which is

1-[((2R,3R,4R)-2-{(1R)-1-[3,5-Bis(trifluoromethyl)phenyl]ethoxy}-tetrahydro-3-(4-fluorophenyl)-2H-pyran-4-yl)methyl]piperazinone, or a pharmaceutically acceptable salt thereof.